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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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ANN R. POKALSKY, ESQ.
NIXON PEABODY LLP
990 STEWART AVENUE
GARDEN CITY, NY 11530-4838

EXAMINER	
COLLINS, CYNTHIA E	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 08/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/530,209	INZE ET AL.	
	Examiner	Art Unit	
	Cynthia Collins	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 May 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-8,27,30-40,42 and 44-51* is/are pending in the application.

4a) Of the above claim(s) *48-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-8,27,30-40,42,44-47 and 51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants' submission filed on December 11, 2003 has been entered.

Claims 1-4, 6-7, 27, 30-31, 34-35, 37-40, 42 and 44-45 were amended in Applicants' submission filed on December 11, 2003.

Claims 48-51 were newly added in Applicants' submission filed on December 11, 2003.

Newly submitted claims 48-50 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: newly submitted claims 48-50 are directed to arresting cell division or preventing re-entry into the cell cycle by reducing the level or activity of a cyclin, which is the subject matter of non-elected Group VI set forth in the restriction requirement mailed September 27, 2001. Accordingly, claims 48-50 are withdrawn from consideration as being directed to a non-elected invention.

Applicants' submission filed on May 24, 2004 has been entered.

Claims 1, 39 and 49 are currently amended in Applicant's submission filed on May 24, 2004 has been entered.

Claims 5, 9-26, 28-29, 41 and 43 are cancelled.

Claims 1-4, 6-8, 27, 30-40, 42 and 44-51 are pending.

Claims 48-50 are withdrawn

Claims 1-4, 6-8, 27, 30-40, 42 and 44-47 and 51 are examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

All previous objections and rejections not set forth below have been withdrawn.

Claim Rejections - 35 USC § 112

Claims 1 and 39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 1 and 39 were amended in Applicants' submission filed on December 11, 2003 to recite the limitation "a DNA molecule encoding an amino acid sequence which is at least 50% identical to the amino acid sequence encoded by the DNA sequence of (a) or (b)". This limitation does not find support in the specification as originally filed, and thus constitutes new matter.

Claims 1 and 39 were amended in Applicants' submission filed on December 11, 2003 to recite the limitation "having the amino acid motif QLLAVACLSLAAKXEET, wherein X is any amino acid and wherein the motif comprises zero or up to two mismatches". This limitation does not find support in the specification as originally filed, and thus constitutes new matter.

Applicants' sequence listing, submitted May 24, 2004 in response to the Offices request to comply with the sequence rules, includes a sequence (SEQ ID NO:5) that does not find support in the specification as originally filed. Accordingly newly submitted SEQ ID NO:5 constitutes new matter.

Claims 1-4, 6-8, 27, 30-37, 39-40, 42 and 44-47 and 51 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the

inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record set forth in the office action mailed June 6, 2003.

Applicants' arguments filed December 11, 2003, have been fully considered but they are not persuasive.

Applicants point to the submitted article of Kono et al., Plant Physiology, July 2003, Vol. 132, pages 1315- 1321, Exhibit A. Applicants submit that the presently claimed isolated DNA molecules encode the same D-Type cyclin of *Arabidopsis* described in Kono et al., i.e., CYCD4;1. Applicants further submit that Kono et al. have demonstrated that CYCD4;1 forms protein complexes with CDKA;1 and CDKB2;1 in insect cells, and the complexes are active in terms of histone H1-activity, demonstrating that CYCD4;1 functions as a cyclin subunit by controlling kinase activities of CDKA;1 and CDKB2;1 in living cells (reply pages 8-9).

The Office acknowledges the teachings Kono et al. (Exhibit A) with respect to the inherent functional properties of CYCD4;1, which corresponds to SEQ ID NO:2. The Office maintains, however, that the teachings of Kono et al. (Exhibit A) are otherwise inapposite to the currently rejected claims, since the currently rejected claims are directed to a genus of sequences that were not described as of Applicants' filing date.

Applicants also point to the amendment of claims 1 and 39 to recite amino acid sequences having at least 50% sequence identity to the amino acid sequence set forth in SEQ ID NO:2 and having the amino acid motif QLLAVACLSLAAIQXEET, wherein X is any amino acid and wherein the motif comprises zero or up to two mismatches. Applicants further point out that they have discovered a new class of D-type cyclin, and have provided means for distinguishing the

class from what was known in the art at the time of filing. In this regard Applicants point to Exhibit 2, a similarity-identity matrix, which is effectively an updated version of Table 1 (reply page 9).

As set forth above, the limitations "a DNA molecule encoding an amino acid sequence which is at least 50% identical to the amino acid sequence encoded by the DNA sequence of (a) or (b)" and "having the amino acid motif QLLAVACLSLAAKXEET, wherein X is any amino acid and wherein the motif comprises zero or up to two mismatches" do not find support in the specification as originally filed and thus constitute new matter. Such sequences are also not considered to be described. The specification does not describe or make reference to a DNA molecule encoding an amino acid sequence which is at least 50% identical to SEQ ID NO:2. The specification also does not describe the amino acid motif QLLAVACLSLAAKXEET, wherein X is any amino acid and wherein the motif comprises zero or up to two mismatches. While Figure 1 illustrates the alignment of SEQ ID NO:2 (CYCD4;1) with CYCD1;1, CYCD2;1 and CYCD3;1, position 14 of the disclosed motif is not occupied by any of the 20 possible amino acids, but by V, M or I only, and the disclosed motif does not comprise up to two unspecified mismatches at up to two unspecified positions, but only the following specific mismatches at the following specific positions: position 3 (V or L), position 4 (S or A), position 6 (S or A), position 12 (S or A), position 14 (V, M or I), and position 17 (T or I). Furthermore, CYCD1;1, CYCD2;1 and CYCD3;1 are not at least 50% identical to SEQ ID NO:2, and the specification does not describe other amino acid sequences that are at least 50% identical to SEQ ID NO:2.

Additionally, Applicants' Exhibit 2 does not support the description of the genus of claimed sequences, as Applicants' Exhibit 2 includes sequences that were either not disclosed in the specification at the time of filing, or not publicly available at the time of filing.

Applicants also point out that out of a whole range of related cyclins, there is only one sequence which has a sequence identity greater than 50% to that of SEQ ID NO:2, Arath-CYCD4;2, which exhibits a 60.1% sequence identity to the sequence set forth in SEQ ID NO:2. The genomic clone carrying CYCD4;2 was deposited in the public database on April 28, 2000 as Accession No. A1.353995. A more recent prediction of CYCD4;2 CDNA was deposited on May 6, 2003, made public on September 16, 2003 as Accession No. NM 121082 (reply pages 9-10).

Applicants observation that out of a whole range of related cyclins only one has a sequence identity greater than 50% to that of SEQ ID NO:2 underscores the Office's assertion that the claimed genus of sequences were not described at the time of filing, since Applicants have disclosed only a single sequence (SEQ ID NO:2), and since the Arath-CYCD4;2 sequence was made public after Applicants' filing date.

Applicants argue that the structure and function of the claimed genus is adequately described in the specification, for example, page 10, lines 6-19, which describes various homologies between cyclins, including those having a 50% identity. Applicant also points to Example 2 which demonstrates that Applicants' D-type cyclin binds both CDC2aAt and CDC2bAt, Example 4 which demonstrates that the native gene encoding Applicants' D type cyclin in induced by cytokinin and/or sucrose, and page 10, lines 4-5 which describe a fragment

comprising amino acid residues 78 to 182 of SEQ ID NO:2 within which is the sequence QLLAVACLSLAAKXEET (amino acid residues 124-140 of SEQ ID NO:2), depicted in Figure 1 (reply page 10).

Regarding page 10, lines 6-19, the Office maintains that page 10 makes only a general reference to the term "substantially homologous", defining it as referring to an undefined "subject", for instance to a nucleic acid, which is at least 50% identical in sequence to an unspecified reference sequence when the entire ORF is compared. The Office also maintains that page 10 does not describe any particular homologies between the nucleotide or amino acid sequences of any particular cyclins.

Regarding Examples 2 and 4, the Office maintains that Examples 2 and 4 support only the description of Applicants' disclosed sequence.

Regarding the sequence QLLAVACLSLAAKXEET as representing the amino acid residues 124-140 of SEQ ID NO:2, the Office maintains that both the sequence listing and Figure 1 describe amino acid residues 124-140 of SEQ ID NO:2 as QLLAVACLSLAAKIEET, not QLLAVACLSLAAKXEET.

The Office maintains that Applicants have not described a representative number of species falling within the scope of the claimed genus that encompasses isolated DNA molecules obtained from any source that encode an amino acid sequence which is at least 50% identical to SEQ ID NO:2 and that have the amino acid motif QLLAVACLSLAAKXEET, wherein X is any amino acid and wherein the motif comprises zero or up to two mismatches, as Applicants have described only a single sequence.

Claims 1-4, 6-8, 27, 30-40, 42 and 44-47 remain rejected, and claim 51 is rejected, under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for the reasons of record set forth below.

Applicants' arguments filed December 11, 2003, have been fully considered but they are not persuasive.

Applicants argue that the claimed invention is enabled in light of the evidence provided by Kono et al., Plant Physiology, July 2003, Vol. 132, pages 1315- 1321, Exhibit A. As discussed with respect to the written description rejection, Applicants submit that the presently claimed isolated DNA molecules encode the same D-Type cyclin of *Arabidopsis* described in Kono et al., i.e., CYCD4;1, and that Kono et al. have demonstrated that CYCD4;1 functions as a cyclin subunit by controlling kinase activities of CDKA;1 and CDKB2;1 in living cells (reply pages 8-9).

With respect to the evidence provided by Kono et al., Plant Physiology, July 2003, Vol. 132, pages 1315- 1321, Exhibit A, and Applicants' submission that the presently claimed isolated DNA molecules encode the same D-Type cyclin of *Arabidopsis* described in Kono et al., i.e., CYCD4;1, the Office acknowledges that Kono et al. have demonstrated that CYCD4;1 functions as a cyclin subunit by controlling kinase activities of CDKA;1 and CDKB2;1 in an insect cell system, but the Office maintains that the claimed invention is not enabled, because the specification does not teach how to successfully use the claimed isolated DNA molecules in an insect cell system, or in any other type of system. Such guidance is necessary because the effect

of using or expressing any isolated DNA molecule in any biological system is unpredictable, as DNA molecules and their encoded polypeptides are subject to different functional constraints in different systems. Absent guidance with respect to how to successfully use the claimed isolated DNA molecules in at least one type of system, it would require undue experimentation for one skilled in the art to determine which system to use (plant, animal, microbial, in vitro, etc.), and how to adapt the claimed isolated DNA molecules for use in that system (choice of vectors, promoters, regulatory sequences, hybridization conditions, etc.). In this regard the Office notes that while Kono et al. successfully used the CYCD4;1 sequence in an insect cell system, they were unsuccessful in their attempts to use the CYCD4;1 sequence in a plant cell system (page 1318 column 2 last paragraph).

Applicants also point out that in response to the assertion that the invention is not enabled for cyclin encoding nucleic acid molecules inducible by any mitogenic agent other than the exemplified sucrose and cytokinin, claims 2, 42, and 45 have been amended to recite "inducible by cytokinin and/or sucrose". Additionally, in response to the assertion that the present invention is allegedly non-enabled for "modulating" the plant cell cycle, plant cell division or growth by modulating the level or activity of a cyclin, claim 38 has been amended to recite "(a) method for promoting plant cell division, plant cell proliferation or growth which comprises increasing the level or activity of a cyclin that binds CDC2a in a plant cell wherein said cyclin comprises the sequence set forth in SEQ ID NO:2", claim 39 has been amended similarly, and claim 40 has been amended to recite "the method of claim 39 wherein increasing the level or activity of the

cyclin that binds CDC2a is achieved by overexpressing one or more of said DNA sequences in a plant cell." (reply pages 11-12).

With respect to Applicants' claim amendments, the Office maintains that the specification does not enable promoting plant cell division, proliferation or growth by increasing the level or activity of a cyclin comprising SEQ ID NO:2. The Office maintains that the claimed invention is not enabled because the specification does not teach how to successfully use the claimed isolated DNA molecules to promote plant cell division, proliferation or growth by increasing the level or activity of a cyclin comprising SEQ ID NO:2, or how to promote plant cell division, proliferation or growth by using other means to increase the level or activity of a cyclin comprising SEQ ID NO:2. Such guidance is necessary because the effect of increasing the level or activity of a cyclin is unpredictable, as cyclin level and activity and effect would be affected by the presence or absence of proteins and other molecules that interact with cyclins or that otherwise function to promote or inhibit plant cell division, proliferation or growth. For example, the activity of a particular cyclin is dependent on the presence of a specific cyclin-dependent kinase, and the activity of a cyclin/ cyclin-dependent kinase complex can be positively or negatively affected by other proteins that specifically bind to or phosphorylate the complex. Absent guidance with respect to how to increase the level or activity of a cyclin comprising SEQ ID NO:2 to promote plant cell division, proliferation or growth, it would require undue experimentation for one skilled in the art to determine which method to use (transformation with DNA, application of protein, etc.), and how to adapt the method (choice of vectors, promoters, regulatory sequences, determination of protein concentration, etc.) in order to achieve the desired results (promotion of plant cell division, proliferation or growth).

Claim 27 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of "may therefore be detected". The term "may" renders the claim indefinite because it is a conditional term, and the conditions under which the labeled DNA molecule may be detected are not specified.

Claims 38, 39 and 40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of "increasing". The term "increasing" renders the claim indefinite because it is a relative term that lacks a comparative basis.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 4, 30-31, 33 and 35-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Soni et al. (Plant Cell. 1995 Jan;7(1):85-103, Applicant's IDS).

The claims are directed to an isolated DNA molecule encoding a cyclin obtained by the method of claim 2 or 3, in which a nucleic acid encoding a cyclin whose native gene is inducible by sucrose and/or cytokinin is obtained by performing a yeast two-hybrid screening assay wherein a cyclin-dependent kinase is expressed as bait and cDNA from a plant cell suspension is expressed as prey. The claims are also directed to an expression vector comprising the DNA

molecule of claim 4, and a host cell comprising the vector of claim 30 or the DNA molecule of claim 4 and a composition comprising the DNA molecule of claim 4.

Soni et al. teach an isolated DNA molecule encoding a cyclin δ3 obtained from *Arabidopsis* by yeast complementation, wherein the native cyclin δ3 gene is inducible by sucrose and/or cytokinin, and is expressed in a plant cell suspension (page 91 Figure 5; page 94 Figure 11; page 95 Figure 12). While Soni et al. do not teach that their DNA molecule was obtained by performing a yeast two-hybrid screening assay, Soni et al. need not teach such a method, since a product-by-process claim may be properly rejected over prior art teaching the same product produced by a different process, if the process of making the product fails to distinguish the two products. See in re Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985). The process of making the claimed product fails to distinguish the two products because the native cyclin δ3 gene is inducible by sucrose and/or cytokinin and is expressed in a plant cell suspension, and would therefore necessarily be obtained by performing a yeast two-hybrid screening assay wherein a cyclin-dependent kinase is expressed as bait, since the ability to bind a cyclin-dependent kinase is an inherent functional characteristic of cyclins. Soni et al. also teach an expression vector comprising the isolated DNA molecule encoding a cyclin δ3, and a yeast host cell comprising the vector and isolated DNA molecule (page 86 column 2 last paragraph - page 87 column 1 first paragraph; page 98 column 2 last paragraph).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (571) 272-0794. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Cynthia Collins

Phuong Bui 8/4/04

PHUONG T. BUI
PRIMARY EXAMINER